

REMARKS / ARGUMENTS

The Claims

In Paper No. 9, Applicants provisionally elected Claims 1-7 and 18. The Examiner has made the restriction requirement final and withdrawn the remaining claims in the application from further consideration.

Applicants hereby cancel Claims 8-17, 19 and 20 without prejudice as being directed to a non-elected invention. Applicants cancel Claims 1-7 and 18 without prejudice. Applicants reserve the right to pursue claims of the same, lesser or greater scope as those cancelled in continuation or divisional applications.

Claims 21-31 have been added. The new claims are fully supported in the specification and do not introduce new matter or raise new issues requiring further consideration and/or search. Entry of the new claims is requested.

Notice to Comply with Sequence Rules, 37 CFR 1.821-1.825

In response to the Notice to Comply with Nucleotide Sequence and/or Amino Acid Sequence Disclosures, Applicants submit herewith a paper copy of the "Sequence Listing", a computer readable form (CRF) thereof, and a statement that the contents of the paper copy and CRF are the same. With this submission, Applicants believe that the application is in compliance with the sequence rules.

Rejections under 35 U.S.C. 112

Claims 1-6 and 18 are rejected as indefinite for containing only the abbreviation "OPG". New Claim 19 recites the term "osteoprotegerin" in conjunction with the abbreviation "OPG".

Claim 18 is rejected as indefinite for reciting "an effective amount" without reference to the function to be achieved. New Claim 31 recites "an amount effective to decrease bone resorption".

Claims 1-4 are rejected as indefinite for reciting the terms "variant" and "derivative". It is alleged that the terms do not have art-recognized meanings and are not adequately defined in the specification and are therefore unclear. Applicants disagree. The definition of "variant" is found at p. 8, lines 19-31 of the specification and the definition of "derivative" is found at p. 8, line 32 to p. 9, line 9 of the specification. It would be clear to one skilled in the art the meaning of the terms "variant" and "derivative"

based on the definitions provided in the specification. The Examiner has not pointed out how the definitions in the specification are inadequate. The rejection should be withdrawn.

Claims 1-6 are rejected under 35 U.S.C. 112, first paragraph as not being enabled. The Examiner argues that only the specific sequences set forth in Claim 7 are enabled and that variants, fragments and derivatives of an OPG protein or an Fc protein are not enabled. Applicants disagree.

There are numerous examples of OPG fragments in the art. For example, the disclosure of PCT application WO97/23614 cited by the Examiner sets forth a number of OPG fragments which have biological activity (see for example Table 1 on pp. 128-129 which reports OPG fragments from residues 22-185 up to residues 22-355). OPG variants are also disclosed. Example 5 of WO97/23614 discloses those residues of OPG that are highly conserved and therefore likely to be important for biological activity. Therefore, it would be apparent to one skilled in the art that the highly conserved residues set forth in Example 5 should be avoided when making amino acid alterations in the OPG polypeptide.

There are numerous examples of Fc fragments and variants in the art such as those set forth on pp. 7-8 of WO98/28427 cited by the Examiner.

Given the guidance in the art, it would not require undue experimentation to make a fusion polypeptide comprising an OPG and an Fc protein either or both of which are a variant, fragment and/or derivative. Sufficient guidance is provided that would enable one to make variants, fragments and or derivatives which retain biological activity.

Rejections under 35 U.S.C.102

Claims 1 and 4 are rejected under 35 U.S.C. 102(b) as being anticipated by Boyle et al. (WO97/23614). Claim 1 is rejected under 35 U.S.C. 102(e) as being anticipated by Boyle et al. (U.S. Patent No. 6,015,938).

The new claims recite a fusion protein comprising an OPG variant or fragment fused at its N-terminus to the C-terminus of an Fc protein. Applicants request withdrawal of the rejection.

Rejection under 35 U.S.C. 103

Claims 1-7 and 18 are rejected under 35 U.S.C. 103(a) as being obvious over Mann et al. (WO98/28427) in view of Boyle et al. (U.S. Patent No. 6,015,938). Mann et al. discloses a fusion protein comprising an Fc and an OB protein, especially a fusion protein having Fc at the amino terminal end. The

Examiner argues it would be obvious to substitute OPG in a fusion protein as taught by Mann et al. Applicants disagree.

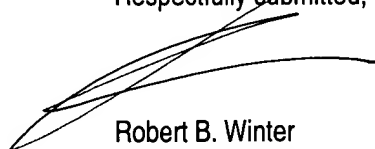
The Examiner's rejection is based on an "obvious to try" assertion and is clearly improper. There is no suggestion in the references that substituting an OPG protein for an OB protein in the disclosed fusion proteins would lead to advantageous properties for the OPG fusion protein. For example, one skilled in the art could not be sure that the fusion of an OPG protein at its amino terminus to the C-terminus of an Fc protein would still retain the biological activity of the OPG protein.

In rejecting the same subject matter under 35 U.S.C. 112, first paragraph, the Examiner argues that it would be unpredictable to make the full scope of claimed fusion proteins of OPG and Fc which have the biological activity of OPG and Fc. It therefore cannot be the case that the claimed fusion proteins would be obvious because one could readily predict the advantageous properties that such proteins would have. Applicants assert that the claimed subject matter is nonobvious and request that the rejection be withdrawn.

CONCLUSION

Claims 21-31 are in condition for allowance and an early notice thereof is solicited.

Respectfully submitted,



Robert B. Winter
Attorney/Agent for Applicant(s)
Registration No.: 34,458
Phone: (805) 447-2425
Date: *NOVEMBER 20, 2001*

Please send all future correspondence to:

U.S. Patent Operations/RBW
Dept. 4300, M/S 27-4-A
AMGEN INC.
One Amgen Center Drive
Thousand Oaks, California 91320-1799